

Blood type and family cancer history in relation to precancerous gastric lesions

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Background	The increased odds of stomach cancer among subjects with blood type A have been reported in epidemiological studies.
Aim	To study the relation of family history of gastric cancer and ABO blood type with precancerous gastric lesions in a high-risk area for stomach cancer.
Subjects and setting	We examined 3400 adults aged 35–64 in a population-based gastric endoscopic screening in a county in China with one of the highest rates of stomach cancer in the world.
Methods	In this cross-sectional study, data on family cancer history, ABO blood type and other characteristics of the participants were obtained by interview and blood test. Responses were compared between those with the most advanced gastric lesions, dysplasia (DYS) or intestinal metaplasia (IM), versus those with chronic atrophic gastritis (CAG) or superficial gastritis (SG).
Results	The prevalence odds ratio (OR) for blood type A relative to other types was 1.39 (95% CI: 1.12–1.73) for DYS and 1.28 (95% CI: 1.06–1.53) for IM. The OR associated with parental history of stomach cancer was 1.88 (95% CI: 1.20–2.95) for DYS, but the numbers were too small to evaluate aggregation among siblings. The combined OR associated with blood type A and a parental history of gastric cancer was 2.61 (95% CI: 1.59–4.30) for DYS and 1.46 (95% CI: 0.93–2.31) for IM.
Conclusions	The findings suggest that genetic factors play a role in developing precancerous gastric lesions.
Keywords	Precancerous gastric lesions, ABO blood type, family stomach cancer history
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Stomach cancer, particularly of the intestinal type, is thought to arise from a series of progressive changes, with transformation of normal mucosa to chronic atrophic gastritis (CAG), intestinal metaplasia (IM), dysplasia (DYS) and eventually cancer.¹ Thus, clues to the causes of stomach cancer may come from studies of precursor lesions whose origins may be influenced by genetic as well as environmental factors. In Linqu, a rural county of China with one of the highest rates of stomach cancer in the world, CAG is nearly universal among adults, while about 50% are also affected with IM and 20% with DYS.^{2,3} To provide leads to genetic factors in gastric carcinogenesis, we examined the

relation between ABO blood type, a history of stomach cancer in a parent or sibling, and precancerous gastric lesions among the 3400 adults participating in a population-based gastroscopic screening survey. Previous studies of stomach cancer have demonstrated an excess risk of gastric cancer associated with blood type A^{4,5} as well as a tendency to familial aggregation.⁶

Materials and Methods

This study is described in detail elsewhere.^{2,3} In brief, a total of 3400 residents aged 35–64 were enrolled in a screening examination in 1989 in 14 villages selected at random, representing 83% of the eligible population.

After health workers visited each person and obtained appropriate written informed consent, the subjects received an endoscopic examination and biopsies were taken from seven standard locations: four from the antrum, one from the angulus, and two from the body of the stomach. The presence or absence of superficial gastritis (SG), CAG, IM and DYS was recorded for each biopsy. Each site was assigned a diagnosis

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Table 1 Prevalence odds ratios (and 95% CI) estimated from logistic regression^a

Blood type A	Parental gastric cancer	IM ^b	DYS ^c
No	No	1.0	1.0
Yes	No	1.28 (1.06–1.53)	1.39 (1.12–1.73)
No	Yes	1.15 (0.75–1.75)	1.88 (1.20–2.95)
Yes	Yes	1.46 (0.93–2.31)	2.61 (1.59–4.30)

^a Adjusted for gender and age (see Methods).^b Intestinal metaplasia.^c Dysplasia.

based on the most severe histology that was found, while each subject was assigned a global diagnosis based on the most severe diagnosis among any of the biopsies. Information on family history, diet and other potential risk factors was obtained by interview, while ABO blood type was determined by a blood test.

Prevalence odds ratios (OR) were used as the measures of association between ABO blood type and gastric lesions in this cross-sectional study. Separate logistic regressions were used to compute OR and 95% CI for DYS versus SG/CAG and for IM (without accompanying DYS) versus SG/CAG (SAS 6.08. Logistic Procedure, SAS Institute, Inc.). The logistic models included the following main effects: a history of parental gastric cancer (1 if present, 0 otherwise), blood type (1 if type A, 0 otherwise), gender (1 if male, 0 if female), and three age categories (35–44, 45–54, 55+).

Results

Among the 3400 adults screened, 13 subjects with screening-detected gastric cancer and 290 with either unavailable ABO blood type or unreported data on family history of cancer were excluded from the analysis. Among 3097 subjects, the ABO blood types of A, B, O or AB were 834 (26.93%), 1059 (34.19%), 920 (29.71%), and 284 (9.17%), respectively.

Blood type was significantly associated with both IM (OR = 1.28; 95% CI: 1.06–1.53) and DYS (OR = 1.39; 95% CI: 1.12–1.73) as shown in row 2 of Table 1. A history of parental gastric cancer was significantly associated with DYS (OR = 1.88; 95% CI: 1.20–2.95), but not with IM. The risks associated with the combination of blood type A and a parental history of gastric cancer were estimated by multiplying the individual OR (row 4, Table 1), yielding an overall OR of 2.61 (95% CI: 1.59–4.30) for DYS and 1.46 (95% CI: 0.93–2.31) for IM. No significant interactions between blood type and parental history were seen (*P*-values = 0.55 and 0.54 for IM and DYS, respectively).

The risk of DYS was also increased among those whose sibling had stomach cancer, but few individuals were affected (data not shown). No evidence was found for an association between parental non-gastric cancer and prevalence of IM or DYS.

Discussion

The increased odds of stomach cancer among subjects with blood type A, after adjusting for parental history of stomach cancer, were of similar magnitude (30–40%) for IM and DYS, suggesting that type A is primarily associated with transitions from CAG to IM with little additional effect on progression to

DYS. In contrast, parental history of gastric cancer, after adjusting for blood type, was associated mainly with DYS, indicating that blood type A and familial tendency may affect different stages of the carcinogenic process.

There have been few epidemiological studies of genetic predisposition to precancerous gastric lesions. In a high-risk area of Colombia, people with blood type A had a higher prevalence of CAG/IM than those with other blood types.⁷ It has been suggested that gastric carcinomas produce antigens immunologically related to blood type A antigens that may help limit tumour growth in non-type A individuals,⁸ but the data from China and Colombia suggest that the influence of blood type A precedes the onset of cancer. It is noteworthy that the putative stage of transition (CAG to IM) affected by type A resembles the pattern observed for Lewis blood-group antigens. In one study, anomalies in Lewis A antigens occurred in 67% of cases with DYS, 65% with IM and only 15% with CAG.⁹

Familial susceptibility has been well documented for stomach cancer⁶ and reported also for CAG in a manner suggesting an autosomal recessive mode of inheritance.¹⁰ Although we had no information on CAG or other precursor lesions among first degree relatives, our data showed that individuals with a parental history of stomach cancer had a significantly higher prevalence of DYS, while the number of siblings with gastric cancer was too small for evaluation.

In summary, this survey of gastric precancerous lesions in a high-risk population in China revealed associations with blood type A and parental history of gastric cancer, consistent with the role of genetic predisposition. Our findings complement earlier studies in this population implicating the effects of dietary practices, cigarette smoking, *Helicobacter pylori* infection, and other environmental factors in the progression of precancerous lesions.^{1,2} Further studies are needed to elucidate genetic mechanisms and gene-environment interactions in the multi-step process of gastric carcinogenesis.

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